Rapid HIV-1 Testing for Women in Labor with Unknown HIV Status: Translating Research & Policy into Practice

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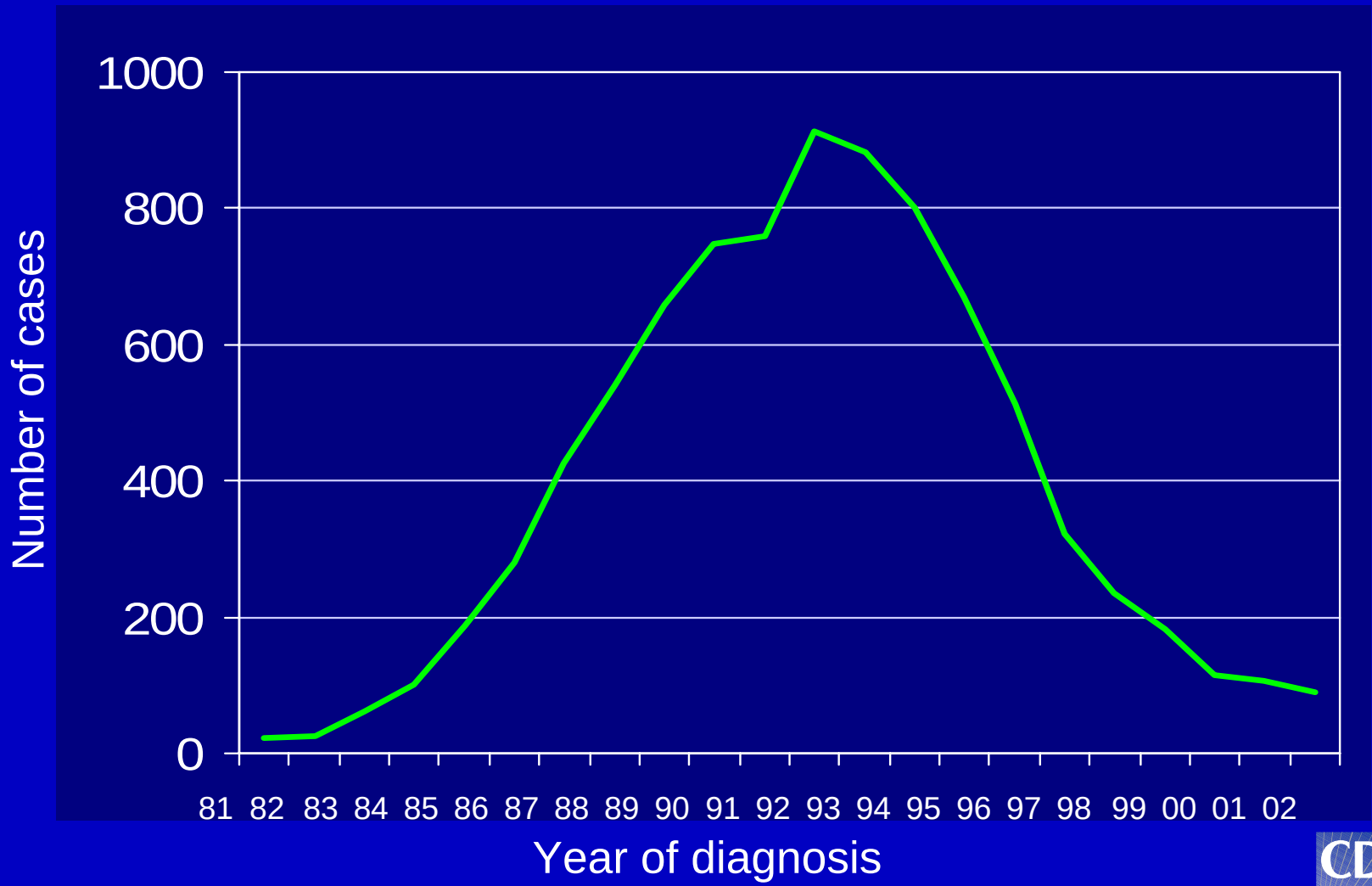
January 20, 2005

Perinatally Acquired **AIDS** Cases by Year of Diagnosis, 1981–2002, United States



Note: Data adjusted for reporting delays and for estimated proportional redistribution of cases reported without a risk.

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AHP Strategy 4
Further Decrease Perinatal HIV Transmission

- Work with partners to promote routine, voluntary prenatal testing, with option to decline (opt-out)
- Develop guidance for using rapid tests during labor and delivery or postpartum and promote its implementation
- Monitor integration of routine prenatal testing and rapid testing at labor and delivery into medical practice
- Case control study to assess why perinatal HIV infections are still occurring

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Prevalence of Diseases Screened for in Newborns

Tyrosinemia:	1 in >300,000
Maple-syrup urine disease:	1 in 175,000
Homocystinuria:	1 in 100,000
Galactosemia:	1 in 60,000
Phenylketonuria:	1 in 14,000
Hypothyroidism:	1 in 4,000
Perinatal HIV exposure, US	1 in 1,500

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Prenatal HIV testing policies

- Voluntary approaches
  - Opt-in: pre-test counseling and written consent specifically for an HIV test
  - Opt-out: notification of test and the option to decline
- Mandatory approaches
  - Mandatory newborn screening: infants are tested, with or without mother's consent, when mother's HIV status is unknown at delivery

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MMWR data sources

- **Chart reviews:**

  8 states, 1998-1999, from a random sample of reviews of prenatal and L&D charts. Active Bacterial Core Surveillance/Emerging Infections Program.

- **PRAMS:**

  9 states, 1999, surveys of a random sample of recently delivered women

- **Lab reports:**

  5 Canadian provinces, 1999-2001, all HIV tests submitted to provincial labs.

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Prenatal HIV Testing by State and Policy, Medical Record Review, 1998-1999

State	Policy	N	%Tested
TN	Opt-out	623	85
NY	Mandatory	438	52
	Mandatory[+]	112	83
CT	Opt-in	668	31
	Mandatory	93	81
MD	Opt-in	665	69
GA	Opt-in	866	66
MN	Opt-in	605	62
CA	Opt-in	575	39
OR	Opt-in	498	25

S. Sansom MMWR, Nov. 2001

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Implementation of Recommended Prenatal Screening Tests, 1998/1999

Test	Frequency (%), (n=5,144)
Hepatitis B	96.5
Syphilis	98.2
Rubella	97.3
HIV	***57.2***

MMWR 2002;51:1013-6

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PRAMS Results, 1999

State	Policy	N	%Tested
FL	Opt-in	1,990	81
NY	Mandatory	758	69
	Mandatory+	502	93
NC	Opt-in	1,770	75
IL	Opt-in	1,994	72
CO	Opt-in	2,039	72
AK	Opt-out	1,892	71
WV	Opt-in	1,327	67
OK	Opt-in	1,980	62
OH	Opt-in	1,589	61

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Prenatal HIV Testing by Canadian Province and Policy, 1999-2001

Province	Policy	N	%Tested
Alberta	Opt-out	37,963	98
New&Lab	Opt-out	4,770	94
Quebec	Opt-in	73,781	83
B Columbia	Opt-in	41,739	80
Ontario	Opt-in	129,758	54

S. King

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Additional conclusions

- Better data needed to assess state perinatal HIV testing rates and timing (ante-, intra-, or post-partum)
  - Ongoing, randomized reviews of medical records may be the most valid approach

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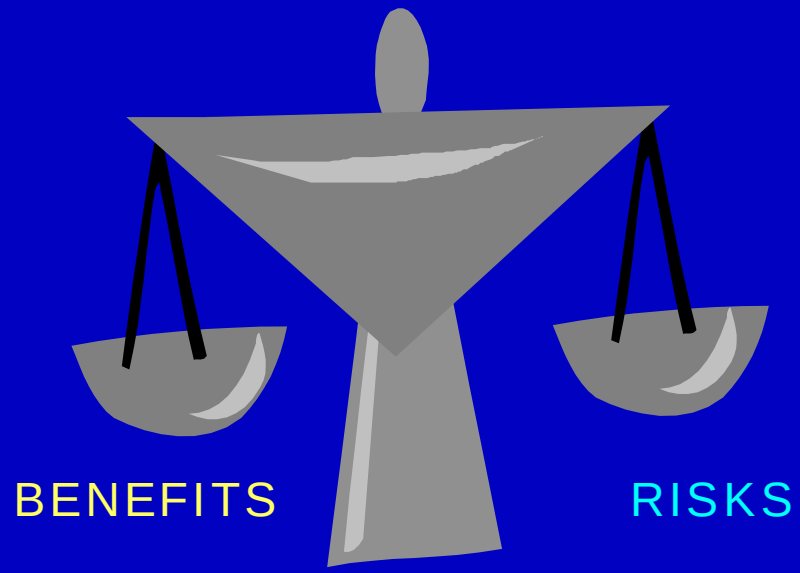
Perinatal HIV Testing Balance Shifting



Benefits versus risks of testing pregnant women for HIV have shifted over years

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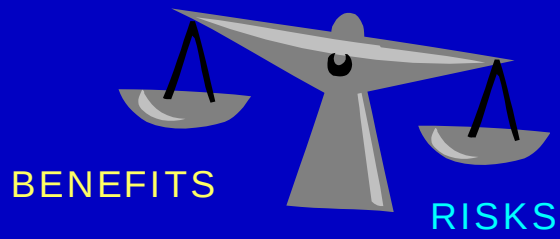
CDC/USPHS Guidelines for Perinatal Testing in the U.S.

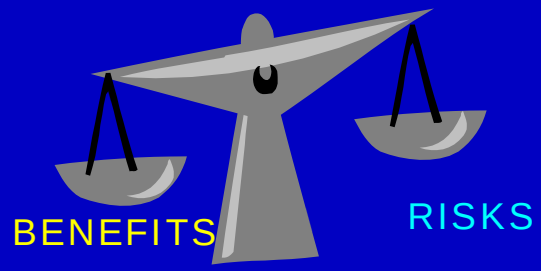
First edition, 1985

- No treatment
- Growing stigma



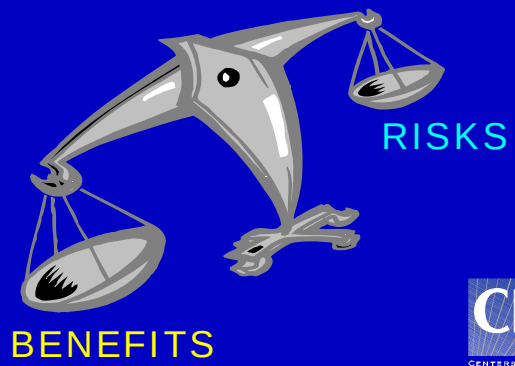
Second edition, 1995

- AZT prophylaxis reduces MTCT
- universal counseling/voluntary testing
- Marked decline in perinatal cases



Third edition, 2001

- Maternal treatment advances allows both mothers and babies to benefit
- "HIV screening should be a routine part of prenatal care for all women."
  - Repeat testing 3rd trimester women at risk and in high prevalence areas
  - **Rapid HIV testing for women in labor with unknown HIV status**



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CDC Recommendations
April 22, 2003

- No child should be born in the U.S. whose HIV status (or mother's status) is unknown
- Routine, opt-out screen prenatally
- Rapid, opt-out test at labor and delivery
- Newborn testing per state law

"Dear Colleague" letter ***www.cdc.gov/hiv/projects/perinatal/***

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ACOG

Committee on Obstetric Practice

Committee Opinion

Number 304, November 2004

Prenatal and Perinatal Human Immunodeficiency Virus Testing: Expanded Recommendations

ABSTRACT: Early identification and treatment of all pregnant women with human immunodeficiency virus (HIV) is the best way to prevent neonatal disease. Pregnant women universally should be tested for HIV infection with patient notification as part of the routine battery of prenatal blood tests unless they decline the test (ie, opt-out approach). Repeat testing in the third trimester and rapid HIV testing at labor and delivery are additional strategies to further reduce the rate of perinatal HIV transmission. The Committee on Obstetric Practice makes the following recommendations: follow an opt-out prenatal HIV testing approach where legally possible; repeat offer of HIV testing in the third trimester to women in areas with high HIV prevalence, women known to be at high risk for HIV infection, and women who declined testing earlier in pregnancy, as allowed by state laws and regulations; use conventional HIV testing for women who are candidates for third-trimester testing; use rapid HIV testing in labor for women with undocumented HIV status; and if a rapid HIV test result is positive, initiate antiretroviral prophylaxis (with consent) without waiting for the results of the confirmatory test.

ACOG Recommendations

- Opt-out prenatal HIV testing
- Repeat HIV testing in 3rd trimester to women:
  - in areas with high HIV prevalence (≥0.5%)
  - known to be at high risk for HIV-infection
  - who declined earlier HIV testing
- Rapid HIV testing for women in labor with undocumented HIV status
  - initiate ARV prophylaxis (with consent) for women with positive results without waiting for confirmatory test results

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Why Rapid HIV Testing for Women in Labor?

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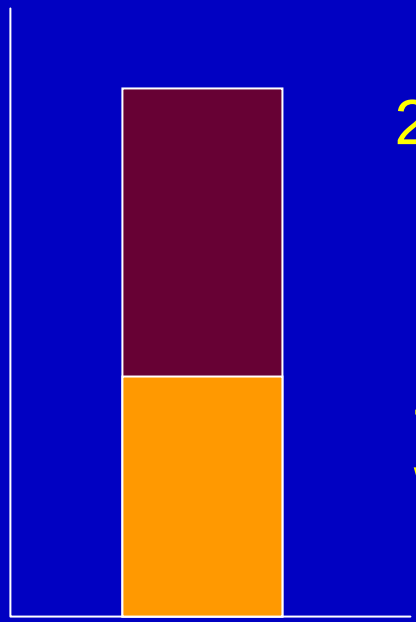
Rationale

- 6,000-7,000 HIV infected women gave birth in 2000



280-370 HIV infected infants

40% of infected infants born to women with unknown HIV status prior to delivery

Office of Inspector General, July 2003

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Rationale

- L&D is an opportunity—a 48 hr window
- 4 FDA-approved Rapid HIV Tests available

1. Oraquick Rapid HIV-1 Antibody Test
2. Reveal G-2 Rapid HIV-1 Antibody Test
3. Uni-Gold Recombigen HIV Test
4. Multispot HIV-1/HIV-2

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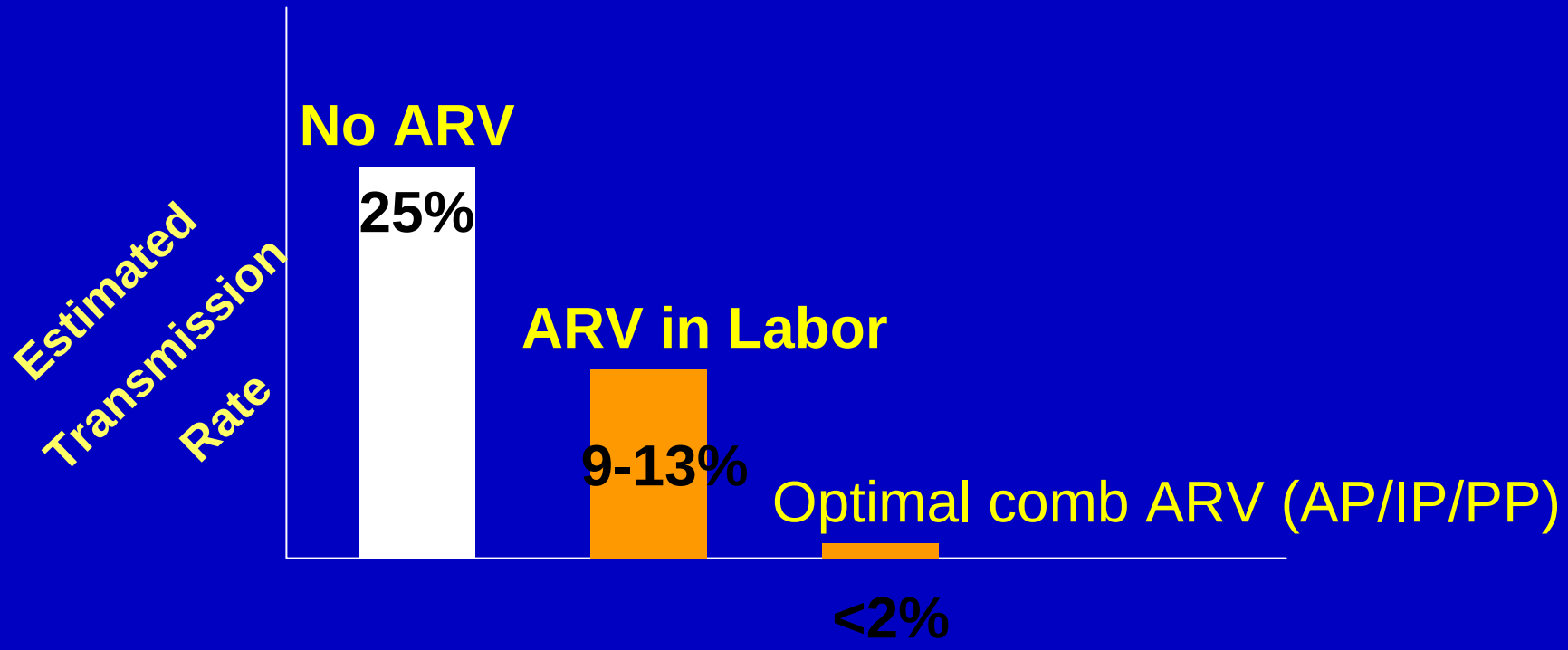
Rationale

An intervention – ARV Prophylaxsis



Wade,et al. 1998 NEJM 339;1409-14
Guay, et al. 1999 Lancet 354;795-802
Fiscus, et al. 2002 Ped Inf Dis J 21;664-668
Moodley, et al. 2003 JID 167;725-735

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P. Garcia

Evidence: Objectives of MIRIAD
Mother Infant Rapid Intervention At Delivery

- To determine the feasibility and performance of rapid HIV testing for women in labor with undocumented HIV status
- To provide timely antiretroviral drug prophylaxis to reduce perinatal transmission
- To facilitate follow-up care for HIV-infected women and their infants

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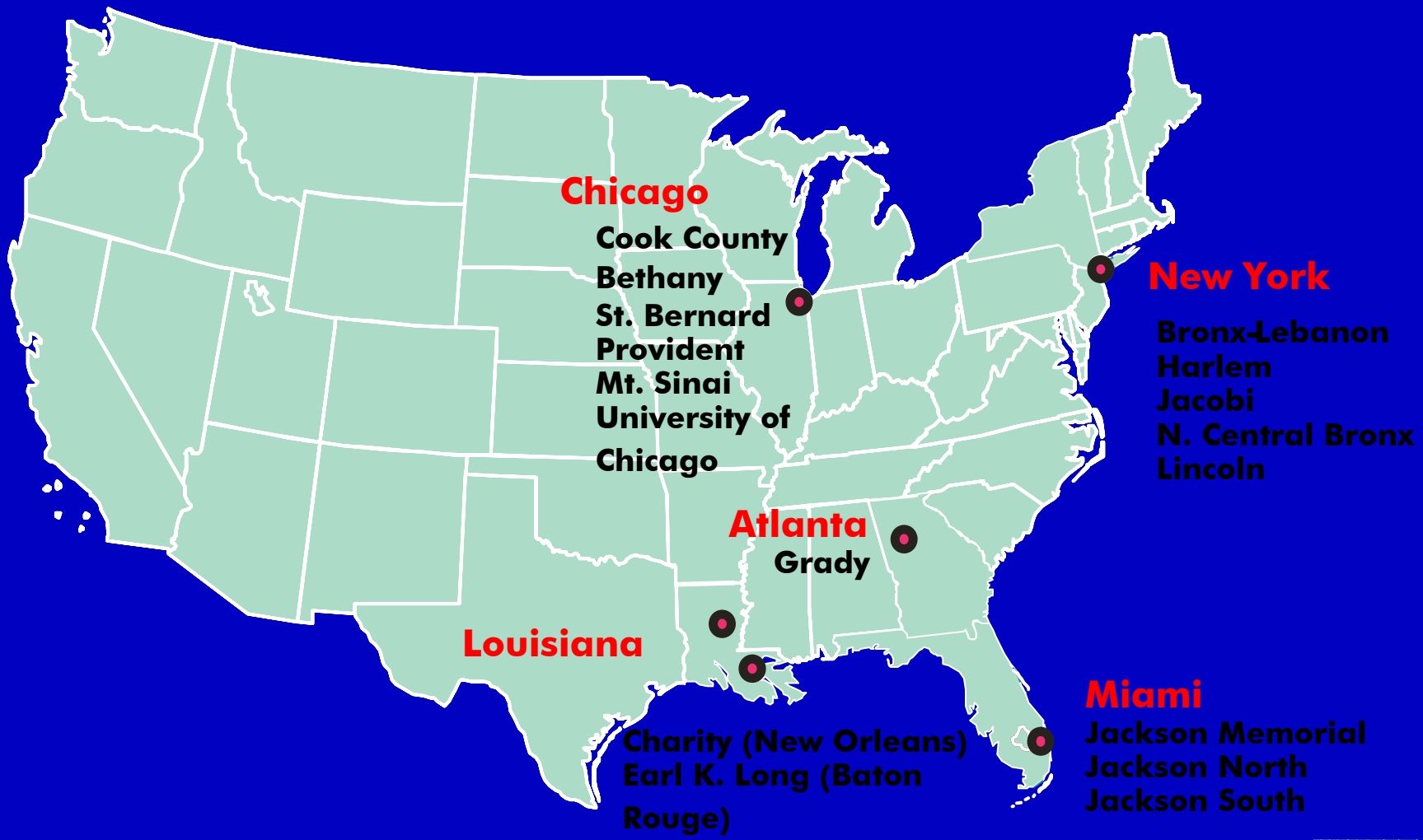
MIRIAD Sites and Hospitals



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MIRIAD Enrollment
(Nov 01-Jun 03)

- **91,707 *encounters* evaluated at 16 hospital L&D units**
- **7,381 women were eligible to participate**
  (no HIV results in records & ≥ 24 weeks gestation)
- **5,744 (78%) approached and offered MIRIAD**
  (rapid HIV testing)
- **4,849 (84%) consented for participation/testing**

Bulterys, et al. JAMA, July 2004—Vol 292, No. 2

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THE BENEFITS OF TAKING AN HIV TEST

- All pregnant women should know if they have HIV.
- You can pass HIV to your baby during pregnancy, childbirth and breastfeeding.
- If you have HIV and are pregnant, you have about a 1 in 4 (25 %) chance of passing HIV to your baby.
- If you have HIV, you can take medicine to keep you healthy and to lower the chances of passing HIV to your baby. You can also choose not to breastfeed since babies can get HIV from their mother's milk.

J Women's Health 2003;12:889-895

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OraQuick Test Performance, MIRIAD (Nov 01- Nov 03)

# False positives	4 *[EIA: 11 false positives]*
# False negatives	0
Sensitivity (95% CI)	100% (90% – 100%)
Specificity (95% CI)	99.9% (99.78% – 99.98%)
Positive Predictive Value	34/38 (90%) *[EIA: 34/45 (76%)]*

Bulterys, et al. JAMA, July 2004—Vol 292, No. 2

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Time to Inform Women of Results MIRIAD
(Nov 01-Jun 03)

	Median	IQ Range
From blood draw	70 min	45 – 125 min
From arrival on L&D	5 hrs	2 – 17 hrs

Bulterys, et al. Abstract #95 11th CROI, Feb 2004

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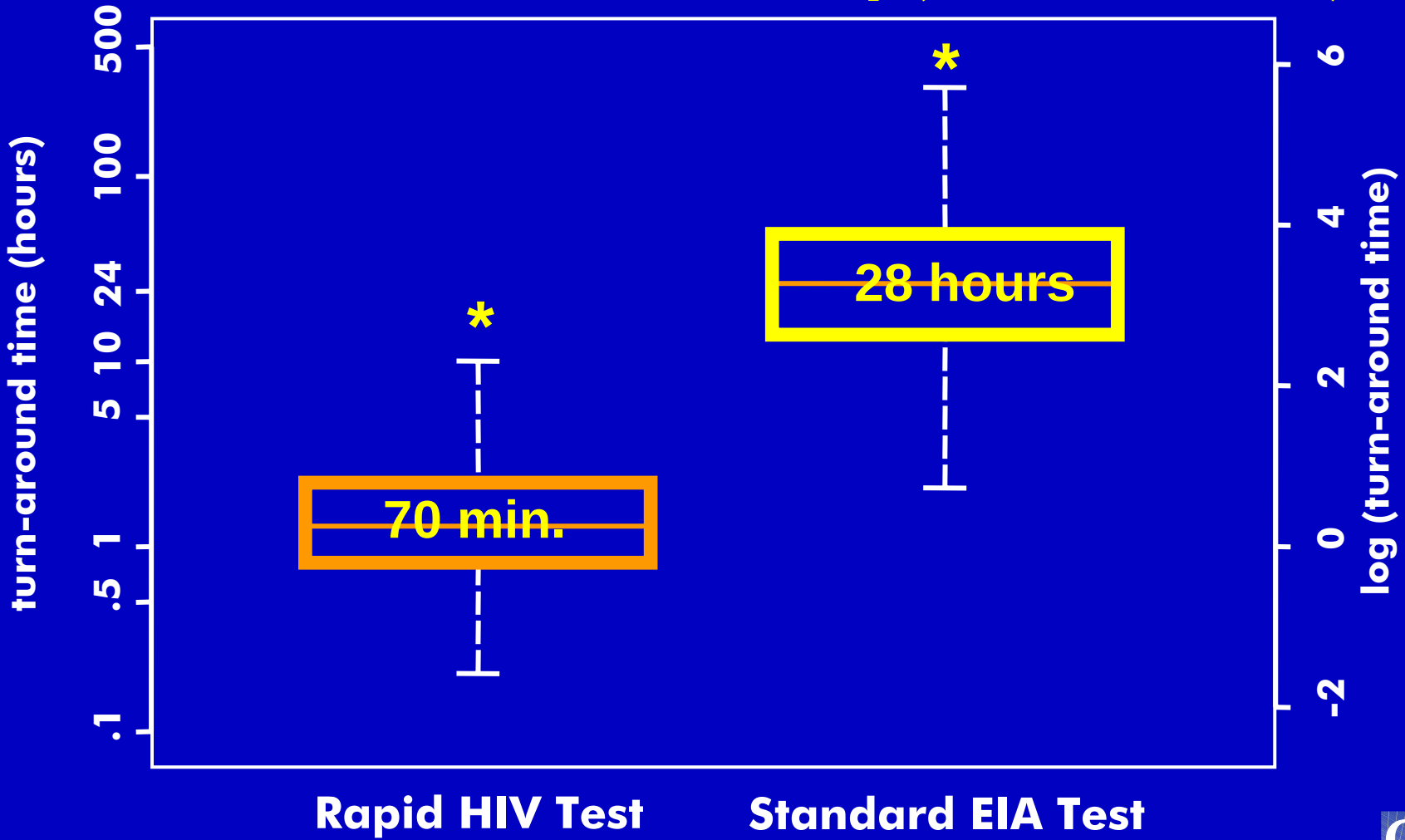
Box plot of rapid HIV testing turn-around times (log scale) compared with standard EIA turn-around times, MIRIAD Study (Nov 01–Jun 03)



Bulterys, et al. Abstract #95 11th CROI, Feb 2004

*Wilcoxon test, p<0.001

Turnaround Times for Rapid Test Results, Point-of-Care vs Lab Testing: MIRIAD

	Median	Range
Point of Care testing (L&D)	45 min	30 – 150 min (.5 – 2.5 hrs)
Laboratory based testing	210 min (3.5 hrs)	94 – 960 min (1.6 – 16 hours)

MMWR 52:36, Sept 16, 2003

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MIRIAD – Lessons Learned

- In laboring women with undocumented HIV status, rapid HIV testing using OraQuick delivered accurate and timely test results
- Acceptance of HIV testing in labor was high but varied by time and day of the week
- Testing performed at the point of care delivered more timely results
- MIRIAD allowed previously unidentified HIV+ women immediate access to intrapartum/neonatal ARV prophylaxis

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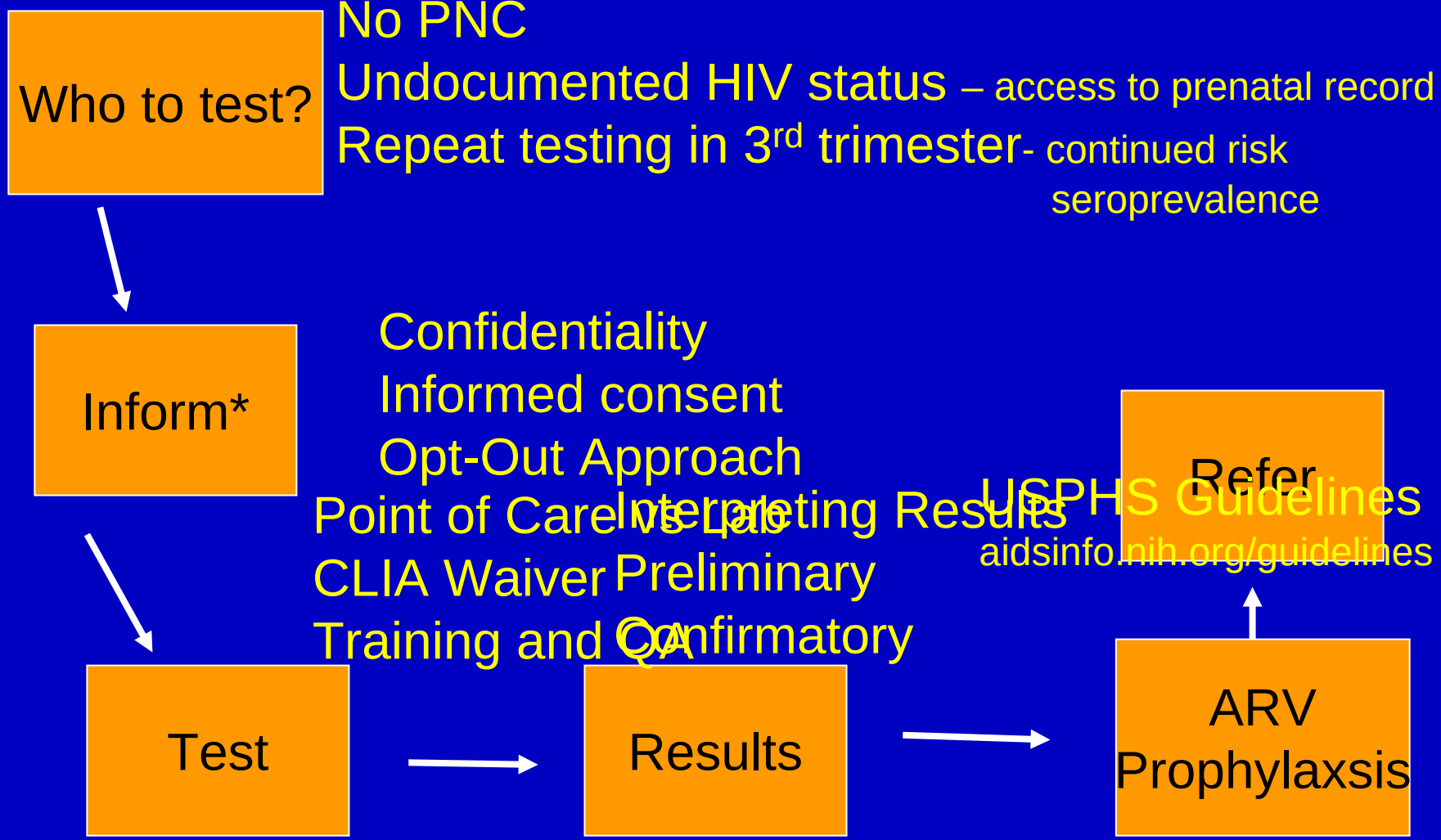
Implementation Considerations



OIG Report: Reducing Obstetrician Barriers to HIV Testing (2002)

"CDC should facilitate the development and states' implementation of protocols for HIV testing during labor and delivery in order to promote testing in this setting as the standard of care."

Office of Inspector General, July 2003

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Perinatal HIV Rapid Testing Protocol Team Convened by CDC

10 individuals with expertise in:

- Obstetrics
- Pediatrics
- Nursing
- Public health practice
- Health education and training
- Blood screening
- Laboratory science
- Epidemiology
- Rapid HIV testing technology
- Care and support of HIV- infected pregnant women

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Rapid HIV-1 Antibody Testing During Labor & Delivery for Women of Unknown HIV Status

A Practical Guide and Model Protocol

January 2004

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Purpose of Model Protocol

- Practical guidance to:
  - Clinicians
  - Laboratorians
  - Hospital Administrators
  - Public Health Professionals
  - Policy Makers
- Provide general structure of a rapid HIV testing protocol, can be adapted locally

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CDC Recommendation

"Hospitals should adopt a policy of routine, rapid HIV testing using an opt-out approach for women who have undocumented HIV test results when presenting to labor & delivery."

Model Protocol: www.cdc.gov/hiv/projects/perinatal

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Medicaid Reimbursement

	CPT Code	Average Reimbursement*
HIV-1 antibody test	**86701**	**$12.41**
CLIA-waived HIV-1 antibody test	**86701QW**	**$12.41**
HIV-1/2 antibody test (single test)	**86703**	**$19.17**

Note: Medicaid reimbursements are determined by states; most (but not all) states reimburse as noted above

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FDA-Approved Rapid HIV Antibody Screening Tests

January 4, 2005

	FDA Approval Received	Specimen Type	CLIA Category*	Sensitivity** (95% CI)	Specificity** (95% CI)	Manufacturer	Approved for HIV-2 Detection?	List Price Per Device^	External Controls
OraQuick Rapid HIV-1 Antibody Test	Nov 2002	Whole blood (fingerstick or venipuncture)	Waived	99.6% (98.5-99.9)	100% (99.7-100)	OraSure Technologies, Inc. www.orasure.com	No	$14.50	Sold Separately ($20 each)
OraQuick ADVANCE Rapid HIV-1/2 Antibody Test	Mar 2004	Oral fluid	Waived	99.3% (98.4-99.7)	99.8% (99.6-99.9)	OraSure Technologies, Inc. www.orasure.com	Yes	$17.50	Sold Separately ($25 each)
		Whole Blood (finger stick or venipuncture)	Waived	99.6% (98.5-99.9)	100% (99.7-100)				
		Plasma	Moderate Complexity	99.6% (98.9-99.8)	99.9% (99.6-99.9)				
Uni-Gold Recombigen HIV	Dec 2003	Whole blood (fingerstick or venipuncture)	Waived	100% (99.5-100)	99.7% (99.0-100)	Trinity Biotech www.unigoldhiv.com	No	$15.75	Sold Separately ($26.25 each)
		Serum & Plasma	Moderate Complexity	100% (99.5-100)	99.8% (99.3-100)				
Reveal G-2 Rapid HIV-1 Antibody Test	Apr 2003	Serum	Moderate Complexity	99.8% (99.5-100)	99.1% (98.8-99.4)	MedMira, Inc. www.medmira.com	No	$14.00	Included
		Plasma	Moderate Complexity	99.8% (99.5-100)	98.6% (98.4-98.8)				
MultiSpot HIV-1/HIV-2 Rapid Test	Nov 2004	Serum	Moderate Complexity	100% (99.94-100)	99.93% (99.79-100)	BioRad Laboratories www.biorad.com	Yes – differentiates HIV-1 from HIV-2	Info not yet available	Included
		Plasma	Moderate Complexity	100% (99.94-100)	99.91% (99.77-100)				

* Clinical Laboratory Improvement Amendments: CLIA regulations identify three categories of tests: waived, moderate complexity, or high complexity

** Sensitivity is the probability that the test result will be reactive if the specimen is a true positive; specificity if the probability that the test result will be nonreactive if the specimen is a true negative. Data are from the FDA summary basis of approval, for HIV-1 only. For HIV-2 information, see package inserts.

^ Actual price may vary by purchasing agreements with manufacturers

Note. Trade names are for identification purposes only and do not imply endorsement.

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National Implementation Plan
Rapid Testing in L&D

1. Promote & market with key partners
2. Train & build capacity
3. Monitor & evaluate
4. Technical Assistance

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Market & Promote with Key National Partners

- **ACOG-** Clinical guidance & published committee opinion (November 2004)
- **HRET(AHA)-** Distribute protocol and promote on-line and via newsletters, annual meetings
- **FXB-** provide materials to AETCs, post on website conduct trainings
  - Regional hospital strategic planning workshops
- **CityMatCH & AMCHP-** city and state MCH public health
- Other partners: ACNM, CAP, Family Physicians

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Monitor & Evaluate

- HRET(AHA) survey
  - Baseline summer ’04
  - Follow-up ’06
- Abstract Sample of Medical Records
  - 8 states in ’04-’05
  - Expand to ~8 additional states in ’05-’06
  - Methodology to all states
  - Contract with RTI

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Technical Assistance

- Funded national organizations
- Direct TA to 16 state perinatal grantees
- Collaborate with HRSA
  - National Perinatal HIV Consultation and Referral Service (Perinatal Hotline)

University of California San Francisco

(888) 488-8765

24 hours/day

7 days/week

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Conclusion

- Until all pregnant women with HIV access screening prenatally, the promise of ACTG 076 and other clinical trials cannot be realized.

- Rapid testing provides a last opportunity to reduce the impact of missed prevention opportunities

Resources

- **National Model Protocol**
  www.cdc.gov/hiv/projects/perinatal/
- **CDC Rapid Testing Site**
  www.cdc.gov/hiv/rapid_testing
- **USPHS Treatment Guidelines**
  www.aidsinfo.nih.gov
- **FXBC at UMDNJ www.WomenChildrenHIV.org**
- **ACOG www.acog.org**
- **AETC http://hab.hrsa.gov/educating.htm**

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